How flu vaccines get to you

The vaccine-manufacturing process begins when the World Health Organization is notified that a research center has detected a virus strain that differs significantly from others that are circulating. The new virus then is sent to one of four "collaborating centers" around the world for analysis and vaccine formulation, including the U.S. Centers for Disease Control and Prevention in Atlanta.

Month 1 | Month 2 | Month 3 | Month 4 | Month 5 | Month 6

World Health Organization/ U.S. Centers for Disease Control

New virus identified

1 Vaccine prep. → 2 Test vaccine virus

WHO issues vaccine indicator
All manufacturers receive a WHO-produced standardized substance (reagents) to measure how much virus is being produced and ensure packaging contains the correct dose

Approval agency
Depending on the country, the vaccine may undergo more testing before it may be distributed

Approval for use

Vaccine indicator development

3 Control → 4 Packaging → 5 Clinical trials

Vaccine manufacturer

1 Test conditions → 2 First batch is ready after two weeks, production continues

Vaccine production
New batches can start once every few days.

Developing a new vaccine

The development of a new influenza vaccine starts when WHO obtains the new strain and adapts it for vaccine manufacturing

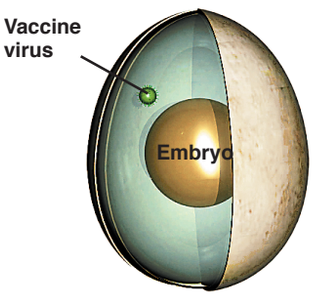
1 Vaccine virus preparation
The new virus is mixed with a standard laboratory virus to make the vaccine less dangerous and better able to grow in a chicken egg

2 Test vaccine virus
The hybrid vaccine virus is tested to make sure it is truly a vaccine, that it is safe and that it grows in eggs

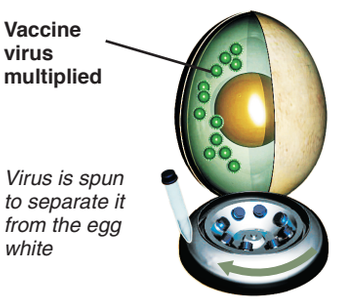
1 2 Vaccine production with chicken eggs

After the hybrid virus has been tested in different growing conditions in eggs, this process is done to thousands of eggs and produces several hundred or thousand liters of purified virus protein, or antigen, which is the active ingredient in the vaccine.

A The vaccine virus is injected into a 9- to 12-day-old fertilized egg and incubated for two to three days; during this time the virus multiplies



B After incubation, the egg white contains millions of vaccine viruses, which are harvested, and then separated from the egg white



C The desired proteins of the virus are purified, tested and eventually bottled as a vaccine

3 Quality control
Manufacturers test each batch of vaccine with the WHO reagents

4 Vaccine packaging
The vaccine is diluted to the proper concentration of antigen, packaged in vials or syringes and labeled; some are tested for sterility, concentration and safety

5 Clinical studies
Vaccine is tested to make sure it performs as expected

FDA approval process

Application
Manufacturers must submit an application describing the vaccine, manufacturing method and quality control tests, as well as information about the vaccine's safety, animal tests results proving effectiveness and a plan for human clinical studies

Human clinical trials
Phase 1 Tests for safety and ability to stimulate an immune response in small number of subjects
Phase 2 Studies dose amount in hundreds of subjects
Phase 3 Provides additional safety data and vaccine effectiveness from tests in thousands of subjects

License application
A license application provides an FDA review team with information needed to make a risk/benefit assessment and to decide whether to recommend the vaccine for approval; the manufacturing facility also undergoes inspection and the vaccine is examined

Committee approval
After the review of a license application, the manufacturer and FDA present the information to a committee of non-FDA experts (the FDA Vaccines and Related Biological Products Advisory Committee) who advise the FDA on safety and efficiency

Distribution
Even after a license is granted, the FDA continues to examine the manufacturing process to ensure safety and effectiveness before the vaccine may be distributed; in some cases the vaccine must undergo a fourth phase of studies

Source: World Health Organization, U.S. Food and Drug Administration, Chicago Tribune
Graphic: Alex Bordens, Chicago Tribune